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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,722	03/06/2006	Tibor Keler	MXI-160US	6148

959 7590 06/24/2008

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
06/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/031,722	KELER ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *65-70* is/are allowed.

6)☒ Claim(s) *51-64 and 71-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/02, 10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed 10/7/2003 is acknowledged. Claims 1-50 were canceled. Clams 51-81 were added.

Claims 51-81 are pending and examined on the merits.

Claim Objections

Claim 63 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 63 is objected to because it is drawn to an antibody of claim 51 which is an antibody fragment or a single chain antibody. Claim 51 is drawn to a human monoclonal antibody. The specification at page 11, lines 22-28 defines antibody as "glycoprotein comprising at least two heavy chains and two light chains interconnected by disulfide bonds." The heavy chain is described as comprising the V_H and the heavy chain constant region. The light chain is described as comprising the V_L and the light chain constant region. Therefore, the structures defined in claim 63 appear to be outside the scope of claim 51.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-64 and 74-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 51 is drawn to an isolated human monoclonal antibody comprising a human heavy chain variable region and a human light chain variable region, wherein each of the heavy and light chains comprises three CDR regions (CDR1, CDR2 and CDR3), where the human antibody binds Her2/neu with an affinity constant (K_A) of at least 10^7M^{-1}, and where the human antibody inhibits growth of a tumor cell expressing Her2/neu, and wherein only the CDR3 regions of each of the heavy and light chains is defined structurally by amino acid sequence. Claim 52, dependent from claim 51 defines structurally only the CDR3 and CDR2 regions of each of the heavy and light chains. Claim 53, dependent from claim 51, defines only the CDR3, CDR2 and CDR1 regions of each of the heavy and light chains. Claim 64 is drawn to an isolated human monoclonal antibody comprising a human heavy chain variable region and a human light chain variable region, wherein the human heavy chain variable region comprises an amino acid sequence selected from the group consisting SEQ ID NO: 2, 6, 10 and sequences that are at least 80% homologous to SEQ ID NOs: 2, 6 and 10; wherein the human light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 4, 8 and 12. In the originally filed claims, the genus of human monoclonal antibodies was defined as

encompassing isolated human monoclonal antibodies which specifically bind to Her2/neu and inhibit growth of cells expressing Her2/neu and produced from a transgenic non-human animal. Subgeneric claims defined human monoclonal antibodies as encompassing those that comprise amino acid sequences shown in SEQ ID NO: 2 and SEQ ID NO: 4 for the IgG heavy chain and kappa light chain variable regions respectively; or amino acid sequences shown in SEQ ID NO: 6 and SEQ ID NO: 8 for the IgG heavy chain and kappa light chain variable regions respectively; or amino acid sequences shown in SEQ ID NO: 10 and SEQ ID NO: 12 for the IgG heavy chain and kappa light chain variable regions respectively. The specification provides a description of the amino acid sequence of the variable regions of three specific human monoclonal antibodies, 3.F2, 1.D2 and 2.E8 (see page 17, lines 13-20).

The newly presented claims are not supported by the originally filed claims or the teachings of the specification because the newly presented claims appear to carve out new subgenera of antibodies defined by CDR3 regions, defined by CDR3 and CDR2 regions, or defined by CDR3, CDR2 and CDR1 regions, or defined by heavy and light chains that were not originally paired together. Further, the newly presented claims are presented in Markush style so that, for example, a CDR3 from a heavy chain of one antibody will be paired with a CDR3 from a light chain of a second antibody. In applicants' remarks that accompanied the preliminary amendment, support was pointed to in the original claims and throughout the specification. Applicants also stated that the CDRs are present within the light and heavy chain variable region sequences as exemplified in the specification and were identified using standard CDR mapping techniques well known to those of ordinary skill in the art. Thus, applicants concluded, the CDRs delineated in the new claims are an inherent feature, recognizable by one of ordinary skill

in the art. This argument is not found persuasive because it does not address the issue at hand, which is that the newly presented claims encompass subject matter that is intermediate in scope between the originally filed broad claim to any human monoclonal antibody that binds to Her2/neu, produced from a transgenic mouse, and the more narrow originally filed claims that defined the structure of the complete variable region of three particular human monoclonal antibodies that bind to Her2/neu. Each of the three particular human monoclonal antibodies that bind to Her2/neu can be viewed as examples of antibodies having at least a heavy chain with a CDR3 and at least a light chain with a CDR3, or antibodies having at least a heavy chain with a CDR3 and a CDR2, and at least a light chain with a CDR3 and a CDR2, or antibodies having having at least a heavy chain with a CDR3, CDR2 and a CDR1, and at least a heavy chain with a CDR3, CDR2 and a CDR1. However, there are no examples provided in the instant specification of functional human monoclonal antibodies that bind to Her2/neu where the CDR3 of the heavy chain, or of the light is out of context of the particular heavy chain variable domain or of the particular light chain variable domain defined for each of the exemplified antibodies. Further, there are no examples provided in the in the instant specification of functional human monoclonal antibodies that bind to Her2/neu where a heavy chain from antibody is paired with a light chain from another antibody. Therefore, the specification and the originally filed claims fail to provide support for the newly presented claimed inventions, and one of skill in the art would not recognize that applicants were in possession the newly defined subgenera of human monoclonal antibodies as defined in the claims.

Claims 51-64 and 74-81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies such as those recited in claims 65-70, where the entire complement of 6 CDRs is defined, does not reasonably provide enablement for claims to antibodies where less than the full complement of 6 CDRs is defined, or where the 6 CDRs are defined in a Markush-type claim where individual heavy and light chains may be mixed and matched, and where the heavy and light chains may be sequences that are at least 80% homologous to SEQ ID NOs: 2, 6 and 10, such as antibodies recited in claim 64. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Claim 51 is drawn to an isolated human monoclonal antibody comprising a human heavy chain variable region and a human light chain variable region, wherein each of the heavy and light chains comprises three CDR regions (CDR1, CDR2 and CDR3), where the human antibody binds Her2/neu with an affinity constant (K_A) of at least $10^7 M^{-1}$, and where the human antibody inhibits growth of a tumor cell expressing Her2/neu, and wherein only the CDR3 regions of each of the heavy and light chains is defined structurally by amino acid sequence. Claim 52,

dependent from claim 51 defines structurally only the CDR3 and CDR2 regions of each of the heavy and light chains. Claim 53, dependent from claim 51, defines only the CDR3, CDR2 and CDR1 regions of each of the heavy and light chains. Claims 54-63 and 74-79 depend from claim 51. Claim 64 is drawn to an isolated human monoclonal antibody comprising a human heavy chain variable region and a human light chain variable region, wherein the human heavy chain variable region comprises an amino acid sequence selected from the group consisting SEQ ID NO: 2, 6, 10 and sequences that are at least 80% homologous to SEQ ID NOs: 2, 6 and 10; wherein the human light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 4, 8 and 12. Claims 80 and 81 are drawn to methods of inhibiting growth of a tumor cell expressing Her2/neu comprising contacting the tumor cell with a human antibody according to claim 51, wherein the tumor cell may be selected from the group consisting of an adenocarcinoma cell, a salivary gland carcinoma, a stomach cancer cell, a kidney cancer, a mammary gland carcinoma cell, a lung carcinoma cell, a squamous cell carcinoma cell and an ovarian cancer cell.

The specification provides the structures of heavy and light chain variable domains of three human monoclonal antibodies that bind to Her2/neu, the antibodies designated as 3.F2, 1.D2 and 2.E8, which are antibodies that fall within the scope of the claims. However, the scope of the claims is much broader than the description of these three monoclonal antibodies. The specification does not provide the structure of any human monoclonal anti-Her2/neu antibody that comprises a heavy chain from one of antibody paired with a light chain of another antibody. The specification does not provide the structure of any human monoclonal antibody that has a CDR sequence substituted with the sequence of a CDR sequence from a second antibody. The

specification does not provide any example of a human monoclonal antibody that where a light chain or a heavy chain sequence has any alteration in it while maintaining binding functionality. Therefore, the specification fails to teach the critical residues required for binding activity.

While the level of skill of those in the antibody arts is high, unpredictability is found in the antibody arts. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff (*Rudikoff et al, Proc Natl Acad Sci USA 1982 Vol 79 page 1979*). Rudikoff teaches that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. Furthermore, while there are some publications that acknowledge that CDR3 is important, the conformations of other CDRs as well as the framework residues influence binding. For example, MacCallum *(MacCallum et al, J. Mol. Biol. (1996) 262, 732-745)* analyzes many different antibodies for interactions with antigen and states that although CDR3 of the heavy and light chain dominate, a number of residues outside the standard CDR definitions make antigen contacts (see page 733, right col) and non-contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (see page 735, left col.). De Pascalis *(De Pascalis et al, The Journal of Immunology (2002) 169, 3076-3084)* demonstrates that grafting of the CDRs into a human framework was performed by grafting CDR residues and maintaining framework residues that were deemed essential for preserving the structural integrity of the antigen binding site (see page 3079, right col.). Although abbreviated CDR residues were used in the constructs, some residues in all 6 CDRs were used for the constructs (see page 3080, left col.). The fact that not just one CDR is essential for antigen binding or maintaining the conformation of the antigen

binding site, is underscored by Casset *(Casset et al, (2003) BBRC 307, 198-205)*, which demonstrates the construction of a peptide mimetic of an anti-CD4 monoclonal antibody binding site by rational design, where the peptide has 27 residues formed by residues from 5 CDRs (see entire document). Casset also states that although CDR H3 is at the center of most if not all antigen interactions, clearly other CDRs play an important role in the recognition process (page 199, left col.). This is demonstrated in this work by using all CDRs except L2 and additionally using a framework residue located just before the H3 (see page 202, left col.). Vajdos (*Vajdos et al. J. Mol. Biol.(2002) 320, 415-428)*, summarizes the generally known relationship between antibody structure and antigen binding, i.e. that antigen binding is primarily mediated by the CDRs in an antibody Fv, while more highly conserved framework segments that connect the CDRs are mainly involved in supporting the CDR loop conformations, but in some cases framework residues also contact antigen (page 416, left col.). Additionally, Vajdos suggest that an important step for understanding how *a particular antibody functions*, it would be useful to assess the contributions of each CDR side chain to antigen binding, and in so doing produce a functional map of the antigen-binding site. In the present case, this is a step that has not be demonstrated by the disclosure of the instant specification for any of the exemplified monoclonal antibodies. Furthermore, Holm (*Holm et al Mol. Immunol., (2007) 44, 1075-1084)* describes the mapping of an anti-cytokeratin antibody where, although residues in the CDR3 of the heavy chain are involved in antigen binding, unexpectedly a residue in CDR2 of the light chain was also involved (abstract). Chen (*Chen et al. J. Mol. Biol. (1999) 293, 865-881)* describes high affinity variant antibodies binding to VEGF where the antigen binding site is almost entirely composed of residues from heavy chain CDRs, CDR-H1, H2, H3 (page 866). Wu (*Wu et al. J.*

Mol. Biol. (1999) 294, 151-162) state that, while certain residues have been identified as important for maintaining conformation, it is difficult to predict which framework residues serve a critical role in maintaining affinity and specificity due in part to the large conformational change in antibodies that accompany antigen binding (page 152 left col.).

In summary, while there may be examples in the art where substitutions in CDRs or in the frameworks have been made and antigen-binding activity is maintained, these substitutions appear to be different for each antibody on a case-by-case basis. Therefore, because the specification lacks any teachings showing examples of antibodies where CDRs have substituted one for another between different monoclonal antibodies, where substitutions have been made anywhere with a heavy and/or a light chain of a given antibody, or where a heavy chain from one antibody has been paired with a light chain from another antibody, one of skill in the art would have to engage in further and undue experimentation to practice the full scope of the claimed invention. The further experimentation would be undue experimentation because, as discussed above, it is not at all clear that for the given antibodies described in the specification as originally filed, that the sequence of the CDR3 is the sole critical element for binding to Her2/neu. With respect to the claims to methods of use of the antibodies of claim 51, because the use of the antibodies requires binding to Her2/neu at the correct epitope of Her2/neu and with the appropriate affinity, the methods of use of claims 80 and 81 are not enabled because the specification does not adequately teach how to make the antibodies of claim 51 having the appropriate binding affinity and specificity as the exemplified antibodies.

Claims 71-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 71-73 are drawn to isolated human monoclonal antibodies that bind to Her2/neu, where the heavy chain variable region is that of a human VH 3-33 gene, and the light chain variable region is that of a human Vk L6 gene; where the heavy chain variable region is that of a human VH 3-23 gene, and the light chain variable region is that of a human Vk L15 gene; or where the heavy chain variable region is that of a human VH 3-33 gene, and the light chain variable region is that of a human Vk L15 gene.

As a preliminary matter, in the remarks accompanying the preliminary amendment filed 10/7/2003 which introduces these claims, applicant fails to specifically point to support in the specification for these new claims. Additionally, upon review of the specification, there does not appear to be any teachings concerning the gene usage of any human antibodies that bind to Her2/neu, nor is there a characterization of the gene usage that resulted in the exemplified monoclonal antibodies. Therefore, one of skill in the art would not find that applicant was in possession of a subgenus of monoclonal human antibodies that bind to Her2/neu and that comprise heavy chain variable regions and light chain variable regions that have the characteristics of the genes listed in claims 71, 72 and 73. Therefore, these claims introduce new matter into the specification as originally filed.

Claims 71-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not teach how to make the human monoclonal antibodies that bind to Her2/neu as claimed, where the structure is characterized by germline sequence origin.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Claims 71-73 are drawn to isolated human monoclonal antibodies that bind to Her2/neu, where the heavy chain variable region is that of a human VH 3-33 gene, and the light chain variable region is that of a human Vk L6 gene; where the heavy chain variable region is that of a human VH 3-23 gene, and the light chain variable region is that of a human Vk L15 gene; or where the heavy chain variable region is that of a human VH 3-33 gene, and the light chain variable region is that of a human Vk L15 gene. Thus, the antibodies encompassed by these claims are characterized by binding specificity and germline sequence origin.

Human immunoglobulin genes are assembled early in B-cell ontogeny by random rearrangement of variable (V), diversity (D), and joining (J) gene segments on the heavy (H) chain locus and V and J on either of the light (L) chain loci. Insertion and deletion of nucleotides

at the junctions of the V, D, and J gene segments create additional diversity. The V gene fragment is responsible for encoding FR1, CDR1, FR2, CDR2 and part of the CDR3. The J gene fragment encodes part of CDR3 and FR4. In heavy chains, the D gene fragment also contributes to CDR3. The diversity of V region genes that are present in the germline can vary considerably.

Bose (*Bose and Sinha, Immunology, 2005. 116:172-183*) teaches that there is a high number of possible antibody species that can be derived from a few germline antibody genes: "The hallmark of cellular immunity is development of a very large antibody repertoire using a handful of germline antibody genes". Therefore, the claimed antibodies encompass large genus of antibody molecules. The diversity is generated by combinatorial association of V, D and J genes and further antigen-driven affinity maturation by somatic mutations across the antibody V regions. Although the exact molecular mechanism of somatic mutations of antibody genes is not elucidated clearly, it is known that the rate of mutations in antibody genes is 10^5-10^6 times more than the normal mutational drift of somatic cells" (page 181, column 1 in particular). David (*David et al, Molecular Immunology, 2007. 44:1342-1351*) teaches that the mutations introduced in an antibody germline sequence as a result of somatic hyper mutation could cause derivatives that have altered affinity for its target (abstract, in particular). The sequence of the unmutated germline form of the antibody can only be guessed.

While the specification demonstrates how to make human monoclonal antibodies that bind to Her2/neu, the specification fails to characterize the exemplified embodiments by their germline origin. It appears from the teachings of David that the determination of the germline origin is not well-established. Further, even if the specification provided statements regarding the germline origin of the exemplified antibodies, it would be unpredictable for one of skill in the art

to make further antibodies with the same germline sequences as stated in the claims, because it is not clear that it is currently well established how to establish the germline sequence of an antibody. Therefore, the specification fails to enable the claimed antibodies.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 51-64 and 74-81 are rejected under 35 U.S.C. 102(b) as being anticipated by Keler (WO 01/09187 A2; published 8 February 2001).

The instant filing date of 3/6/2006 is used as the filing date for comparison with the prior art for claims 51-64 and 74-81, because these claims are not supported by the parent applications PCT/US00/20272, 60/146,313 and 60/188,539. For the reasons set forth above in the rejection of the claims for introducing new matter into the specification as originally filed, claims 51-64 and 74-81 are denied priority.

Keler teaches isolated human monoclonal antibodies 3.F2, 1.D2, and 2.E8 which comprised the following heavy and light chain pairs, respectively: SEQ ID NO: 2 paired with SEQ ID NO: 4 (3.F2); SEQ ID NO: 6 paired with SEQ ID NO: 8 (1.D2); and SEQ ID NO: 10 paired with SEQ ID NO: 12 (2.E8). Therefore, Keler teaches antibodies with the scope of claims 51-53. Keler also teaches an antibody produced from a transgenic non-human animal (page 2,

lines 16-17). Keler teaches an antibody that mediates cytolysis (page 3, lines 17-18). Keler teaches antibodies with the affinity constants listed in claims 56 and 57 (page 3, lines 10-12). Keler teaches antibodies with a dissociation rate constant of about $10^{-3}S^{-1}$ or less (page 2, lines 29-30). Keler teaches antibodies that inhibit the growth of tumor cells selected from the group consisting of an adenocarcinoma cell, a salivary gland carcinoma, a stomach cancer cell, a kidney cancer, a mammary gland carcinoma cell, a lung carcinoma cell, a squamous cell carcinoma cell and an ovarian cancer cell (page 3, lines 6-9). Keler teaches a therapeutic dosage of antibodies that inhibits tumor cell growth by at least about 60% (page 50, lines 24-26). Keler teaches monclonal human antibodies 3.F2 and 2.E8 that do not bind to A431 cell that express high levels of EGFR (page 63, lines11-14). Keler teaches antibody fragments of the antibodies of claim 51 (page 63, line 27-29). Keler teaches monoclonal antibodies 3.F2, 2.E8 and 1.D2 that are IgG1 antibodies (page 62, lines 15-17). Keler teaches a composition comprising the antibody of claim 51 and a pharmaceutical carrier (page 43, lines 19-22). Keler teaches an immunoconjugate comprising the antibody of claim 51 linked to a therapeutic agent, where the therapeutic agent maybe a cytotoxin, or may be in a composition comprising a pharmaceutically acceptable carrier (page 42, lines 7-10; page 43, lines 19-26). Keler teaches bispecific antibodies comprising the antibody of claim 51 and a second binding specificity for an Fc receptor (page 34, line 27- page 42, line 4). Keler teaches methods of inhibiting the growth of tumor cells expressing Her2/neu compising contacting the tumor cell with a human antibody according to clam 51, where the tumor cell is selected from the group consisting of an adenocarcinoma cell, a salivary gland carcinoma, a stomach cancer cell, a kidney cancer, a mammary gland carcinoma cell, a lung carcinoma cell, a squamous cell carcinoma cell and an ovarian cancer cell (page 63,

line 20 - page 64, line 2). Therefore, Keler teaches antibodies and methods that are the same as that claimed.

Conclusion

Claims 65-70 are allowed. Claims 51-64 and 71-81 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
June 19, 2008

/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643